DETAILED ACTION

The amendment filed December 22, 2009 (hereinafter referred to as "the response") has been entered. Claim 17 has been amended and Claims 51 and 52 have been newly added.

Accordingly, Claims 17-20, 51, and 52 are pending in the instant application

The elected invention is drawn to a tumor cell composition comprising a tumor cell modified to express a B7-2 protein and at least one additional immune modulator, or a functional fragment of said B7-2 protein or said immune modulator. Applicants further elected GM-CSF as the cytokine species for prosecution.

Accordingly, Claims 17-20, 51, and 52 are examined herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17, 51, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,548,068 (Schlom et al., priority to 6/7/95) and Dranoff et al. (1993, Proc. Natl. Acad. Sci. USA 90: 3539-3543).

The claims are directed to a tumor cell composition consisting of an isolated primary tumor cell modified to express a B7-2 protein and at least one additional immune modulator, wherein said isolated primary tumor cell expressing B7-2 and at least one immune modulator has been irradiated. Dependent claims further specify that the immune modulator is a cytokine and that the cytokine is GM-CSF. Claim 52 is directed to a tumor cell composition comprising an isolated autologous primary tumor cell

transfected to express a B7-2 protein and GM-CSF, wherein said isolated autologous primary tumor cell expressing B7-2 and GM-CSF has been irradiated.

Schlom et al. disclose and claim a tumor cell modified to express B7-2 and GM-CSF. See especially Claims 1, 4, and 5. Claim 1 is directed to a host cell infected with a recombinant vaccinia virus which has incorporated into the viral genome a gene or portion thereof encoding B7-2. The claim further specifies that the B7-2 gene is expressed. Claim 4 is directed to the host cell according to Claim 1 wherein the recombinant virus further comprises one or more genes or portion thereof encoding an immunostimulatory molecule selected from the group consisting of IL-2, ICAM-1, LFA-3, CD72, GM-CSF, TNFα, INFγ, IL-12, IL-6 and combinations thereof. Claim 5 is directed to the host cell according to any one of Claims 1 to 4 "wherein the host cell is …a tumor cell …" Thus, the patent clearly discloses a tumor cell modified to express both B7-2 and GM-CSF, as instantly claimed. The reference further discloses that the recombinant vaccine composition may be used for gene therapy and that such an approach requires using cells from a given patient, inserting a gene encoding an immunostimulatory molecule such as B7-1, B7-2, IL-2, or GM-CSF into those cells, and administering the cultured cells back to the patient (column 1, lines 40-45). Thus, the patient receives genetically-modified autologous cells which minimizes or eliminates immunorejection of the introduced cells. This approach clearly discloses the production of an isolated primary tumor cell modified to express a B7-2 protein and at least one additional immune modulator, as instantly claimed.

Dranoff et al. (1993) disclose that irradiated tumor cells expressing murine GM-CSF stimulated potent, long-lasting, and specific anti-tumor immunity (abstract). With regard to the use of autologous cells, the reference further states that "the use of autologous cancer cells as vaccines to augment anti-tumor immunity has been explored throughout this century" (page 3539, column 1, paragraph 1). With regard to the use of irradiated cells and primary tumor cells, the reference further teaches "to the extent that either the *in vitro* manipulation of tumor cells or retroviral integration might pose the risk of

conferring a more malignant phenotype upon the transduced cells, the use of irradiated rather than live cells as cancer vaccines would appear to be extremely important. Moreover, since primary tumor explants likely contain nonneoplatic elements as well, irradiation of the tumor samples before vaccination will also prevent the possibility of the autonomous growth of nonneoplastic cells induced by autocrine synthesis of their own growth factors" (page 3543, column 1, paragraph 2).

Given that Dranoff et al. teaches a distinct advantage to using irradiated primary tumor cells rather than live cells as cancer vaccines, one of skill in the art would have been clearly motivated to irradiate the tumor cell compositions of Schlom et al. to avoid the risk of introducing cells with a malignant phenotype and to avoid the growth of nonneoplastic cells that may be present in a composition produced from a primary tumor explant.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

At page 5 of the response, Applicanst assert that Schlom does not disclose isolated primary tumor cells that have been modified to express B7-2 proteins and at least one additional immune modulator, wherein the isolated primary tumor cell expressing B7-2 and at least one additional immune modulator has been irradiated. However, Dranoff et al. (1993) teaches this limitation and the distinct advantage of using irradiated primary tumor cells rather than live cells as cancer vaccines. Accordingly, the argument is moot in view of the rejection under 35 U.S.C. 103.

At page 6 of the response, Applicants assert that Schlom is not enabling for isolated primary tumor cells that have been modified to express B7-2 proteins and at least one additional immune modulator, wherein the isolated primary tumor cell expressing B7-2 and at least one immune modulator. Applicants continue to argue that Schlom discloses that tumor cells "expressing both the tumor associated antigen along with an immunostimulatory molecule are administered to a mammal in an effective amount to result in tumor reduction or elimination in the mammal afflicted with cancer" (citing column 13, line

64 to column 14, line 4 of Schlom). Applicants further contend that Schlom does not provide any specific examples of such tumor cells containing these components or of their use as immunogenic compositions. However, reduction to practice is not required to enable the disclosed tumor cell compositions, as transduction of tumor cells with recombinant virus encoding the B7-2 and GM-CSF proteins is fully enabled given the advanced state of the art for transducing cells with viral vectors. Furthermore, the composition claims are issued in a U.S. Patent and therefore are understood to be fully enabled.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

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